Clinical Policy: Selumetinib (Koselugo)

Reference Number: CP.PHAR.464
Effective Date: 04.10.20
Last Review Date: 02.22
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Selumetinib (Koselugo™) is a mitogen-activated protein kinase enzyme 1/2 inhibitor.

FDA Approved Indication(s)

Koselugo is indicated for the treatment of pediatric patients 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas (PN).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Koselugo is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Neurofibromatosis Type 1 (must meet all)**:**

1. Diagnosis of NF1;
2. Prescribed by or in consultation with an oncologist or neurologist;
3. Age between 2 and 18 years at start of therapy (*see Appendix F*);
4. For Koselugo requests, member must use selumetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Member has body surface area ≥ 0.55 m^2;
6. Member has at least one inoperable and measurable PN, defined as a lesion ≥ 3 cm measured in one dimension;
7. Member meets one of the following (a or b):
   a. Positive genetic testing for NF1;
   b. Member has at least one other diagnostic criterion for NF1 (*see Appendix D*);
8. Complete resection of PN is not considered to be feasible without substantial risk or morbidity (e.g., due to encasement of, or close proximity to, vital structures, invasiveness, or high vascularity of the PN);
9. Dose does not exceed 100 mg (4 capsules) per day.

Approval duration: 6 months

B. Glioma (off-label) (must meet all):

1. Diagnosis of WHO Grade 1 or 2 pilocytic astrocytoma;
2. Prescribed by or in consultation with an oncologist;

3. Disease is recurrent or progressive;
4. Documentation of BRAF fusion or BRAF V600E activating mutation;
5. For Koselugo requests, member must use selumetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 100 mg (4 capsules) per day.
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Neurofibromatosis Type 1 (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Koselugo for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy as evidenced by decreased or maintained volume of PN(s) from baseline;
3. For Koselugo requests, member must use selumetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, new dose does not exceed 100 mg (4 capsules) per day.

Approval duration: 12 months

B. Glioma (off-label) (must meet all):

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Koselugo for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;

3. For Koselugo requests, member must use selumetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. Request meets one of the following (a or b):*
   a. Dose does not exceed 100 mg (4 capsules) per day.
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
NF1: neurofibromatosis type 1
PN: plexiform neurofibroma

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: National Institutes of Health: Neurofibromatosis 1 Diagnostic Criterion

- Six or more café-au-lait macules (greater than or equal to 0.5 cm in prepubertal subjects or greater than or equal to 1.5 cm in post pubertal subjects)

- Freckling in axilla or groin
- Optic glioma
- Two or more Lisch nodules
- A distinctive bony lesion (dysplasia of the sphenoid bone or dysplasia or thinning of long bone cortex)
- A first-degree relative with NF1

Appendix E: Recommended Dosage Based on Body Surface Area

Body Surface Area	Recommended Dosage
0.55 – 0.69 m^2	20 mg in the morning and 10 mg in the evening
0.70 – 0.89 m^2	20 mg twice daily
0.90 – 1.09 m^2	25 mg twice daily
1.10 – 1.29 m^2	30 mg twice daily
1.30 – 1.49 m^2	35 mg twice daily
1.50 – 1.69 m^2	40 mg twice daily
1.70 – 1.89 m^2	45 mg twice daily
≥ 1.90 m^2	50 mg twice daily

Appendix F: General information

- FDA approval was based on SPRINT II (NCT01362803): Phase II Stratum 1 clinical trial. Eligible patients were 2-18 years of age with NF1 who had inoperable PN. Study consisted of 50 children ages 2-18, median age 10.2 (3.5-17.4).

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NF1	25 mg/m^2 PO BID	100 mg/day

VI. Product Availability

Capsules: 10 mg, 25 mg

VII. References

1. Koselugo Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; April 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213756s000lbl.pdf. Accessed November 24, 2021.
2. Selumetinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 24, 2021.
3. Dombi E, Baldwin A, Marcus L, et al. Activity of selumetinib in neurofibromatosis type-1 related plexiform neurofibromas. N Engl J Med. 2016; 375(26): 2550-2560.
4. Gross AM, Wolters P, Baldwin A et al. SPRINT: Phase II study of the MEK ½ inhibitor selumetinib (AZD6244, ARRY142886) in children with neurofibromatosis type 1 (NF1) and inoperable plexiform neurofibromas (PN). Journal of Clinical Oncology. 2018; 36(15): 10503. Available from: http://ascopubs.org/doi/abs/10.1200/JCO.2018.36.15_suppl.10503. Accessed November 16, , 2021.

5. National Institutes of Health Consensus Development Conference Statement: neurofibromatosis. Bethesda, Md., USA, July 13-15, 1987. Neurofibromatosis 1:172-178, 1988
6. Miller DT, Freedenberg D, Schorry E, et al. Health Supervision for Children With Neurofibromatosis Type 1. Pediatrics. 2019;143(5):e20190660

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	01.09.20	02.20
Drug is now FDA approved - criteria updated per FDA labeling; modified prescriber restriction to indicate that Koselugo can be prescribed by neurologist and oncologist; expanded age restriction; added Appendix E: Recommended Dosage Based on Body Surface Area; references reviewed and updated.	04.21.20	05.20
1Q 2021 annual review: clarified PNs are inoperable as per FDA label; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	11.25.20	02.21
1Q 2022 annual review: added off-label use for low grade glioma per CNS cancers NCCN guidelines version 2.2021; added requirement for use of generic product if available; references reviewed and updated.	11.16.21	02.22
Template changes applied to other diagnoses/indications.	09.28.22	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.